Remarks

Claims 1-40 are pending. Claims 1-12 are under examination and have been rejected. Claims 13-40 have been withdrawn from consideration pursuant to a restriction requirement.

Information Disclosure Statements

The record of the application contains four separate Information Disclosure Statements filed by applicants. Each Statement was duly received by the Office, as each appears in the file of the application. Examiner is respectfully requested to initial the references listed on the PTO Form 1449 that accompanied each Statement, and return the set of four examiner-initialed PTO Forms 1449 to the undersigned with the next disposition of the application.

Response to the Rejections

(1) Rejection of Claims 2 and 7 under 35 U.S.C. § 112 Second Paragraph.

The examiner has again rejected claims 2 and 7 under 35 U.S.C. § 112 for being allegedly indefinite in the recitation of the term "substantially free" as applied to the optical purity of the (*R*) and (*S*) enantiomers. The applicants respectfully traverse the rejection.

At page 8 of the Detailed Action, Examiner alleges that it is unclear from the claim language what applicant means by "substantially free", i.e., "is it free or is it not free of the enantiomer". Applicants again respectfully point out that the term "substantially free" is, in fact, explicitly defined in the specification (see p. 17 lines 9-13), which states that an enantiomer "substantially free" *of the other enantiomer* means that the composition comprises 80% or more by weight of the enantiomer of interest (and thus, by implication, 20% or less of the other enantiomer). The meaning of the term is perfectly clear when interpreted in light of the specification. Reconsideration and withdrawal of the Section 112 rejection is again respectfully requested.

(2) Rejection of Claims 1 and 12 under 35 U.S.C. § 102(b).

Examiner has rejected claims 1 and 12 under 35 U.S.C. § 102(b) as being allegedly anticipated by Korosi *et al.* US Pat. 4,423,044 (hereinafter "Korosi '044"). The applicants respectfully traverse the rejection.

Examiner states that Korosi '044 is anticipatory because it discloses 3,4-dihydro-5H-2,3-benzodiazepine derivatives of a formula I. The Examiner appears to allege that because one can conceivably pick and choose among the various substituent definitions for R, R^1, R^2, and R^3 of formula I and arrive at the compound 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine, the claimed invention is anticipated. This is an incorrect statement of the law.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP 2131 citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). MPEP 2131.01. Moreover, the single source must disclose all of the claimed elements "arranged as in the claims" *Richardson v. Suzuki Motor Co.* 9 USPQ2d 1913, 1920 (Fed, Cir. 1989). For anticipation, a reference must "clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without any need for picking, choosing, and combining various disclosures..." *In re Arkley*, 172 USPQ 524, 526 (CCPA 1972). Anticipation is not made out by hindsight selection based on an applicant's disclosure of variables of a broad generic disclosure. *In re Ruschig*, 145 USPQ 274 (CCPA 1965); *Ex parte Garvey*, 41 USPQ 583 (Bd. of Pat. Appeals 1939).

Korosi '044 does not disclose the compound 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine by name or structure. In order to arrive at that compound from the reference disclosure, one must select ethyl for R^1, methoxy for R^2 and R^3, and 3-hydroxy-4-methoxyphenyl for R in formula I of the reference.

Korosi '044 therefore doe not "clearly and unequivocally" disclose 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine. Nor does Korosi '044 direct one to that compound without any need for picking, choosing, and combining various portions of the reference disclosure. It is only with hindsight and the benefit of applicants' disclosure that one would be led to a pharmaceutical composition comprising 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine. Korosi '044 does not anticipate claim 1 or 12.

Reconsideration and withdrawal of the rejection of claims 1 and 12 under 35 U.S.C. § 102(b) is therefore respectfully requested.

(3) Rejection of Claims 2-11 under 35 U.S.C. § 103(a).

The examiner has rejected claims 2-11 under 35 U.S.C. § 103(a) as being allegedly unpatentable for obviousness over Korosi '044. The applicants respectfully traverse the rejection.

The examiner states that the difference between claims 2-11 and Korosi '044 is that applicants claim the R and S isomer, "whereas the prior art", i.e. Korosi '044, "discloses the racemate". For the reasons discussed above, Korosi '044 does not disclose the racemate of 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine. As such the preparation of the R or S isomer of 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine can not be obvious from Korosi '044, since the alleged modification of that reference, isolation of an R or S isomer, does not result in the invention of any of claims 2-11.

Based on the foregoing, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

(4) Rejection of Claims 1-6 for Alleged Obviousness Type Double Patenting.

The examiner has continued the rejection of claims 1-6 for alleged obviousness-type double patenting over claim 5 of U.S. Patent No. 6,864,251 (the '251 patent), claim 5 of U.S. Patent Application Serial No. 10/309,573 (the '573 application), claim 13 of U.S. Patent Application Serial No. 10/727,940 (the '940 application) and claim 6 of U.S. Patent Application Serial No. 10/728,286 (the '286 application), each of which are said to claim methods of treatment using 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine.

Applicants once more respectfully point out that the rejection over the '573 application is improper because it is duplicative of the rejection over the '251 patent since the '573 application is the application which resulted in the issuance of the '251 patent. Withdrawal of the double patenting rejection as it relates to the '573 application is respectfully requested.

The rejection over the '286 application is likewise improper, since that application was been abandoned. Examiner's attention is directed to the Notice of Abandonment mailed Nov. 16, 2007 in that application.

Applicants again respectfully point out that the rejection for double patenting over claim 13 of the '940 application is premature since the allegedly conflicting claim has not yet been patented. The claims of the present application should therefore have been rejected only *provisionally*. The office action does not so indicate that the double patenting rejection over the '940 application is provisional.

Conclusion.

Based on the foregoing, applicants respectfully submit that the rejections under 35 U.S.C. §§ 102(b), 103(a) and 112 have been overcome. In addition, the applicants respectfully remind the examiner of the eligibility of the dependent process claims 13-40 for rejoinder under MPEP 821.04 when claim 1 is placed in condition for allowance.

Respectfully submitted

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